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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/870,128 | 05/30/2001 | Oystein Ihle | 4290-4000 | 6505 |

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| EXAMINER | |
|---|---|
| CALAMITA, HEATHER | |
| ART UNIT | PAPER NUMBER |
| 1637 | |

DATE MAILED: 04/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/870,128 | IHLE ET AL. | |
| | Examiner | Art Unit | |
| | Heather G. Calamita, Ph.D. | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *39-80,82,89,91 and 94-100* is/are pending in the application.

4a) Of the above claim(s) *59-61,63-79 and 94-96* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-58, 62, 80, 82, 89, 91, 97-100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/07/02, 08/09/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of Application, Amendments, and/or Claims*

1. Claims 39-80, 82, 89, 91 and 94-100 are pending. Claims 39-58, 62, 80, 82, 89, 91, 97-100 are under examination. All arguments have been fully considered and thoroughly reviewed, but are deemed not persuasive for the reasons that follow. Any objections and rejections not reiterated below are hereby withdrawn.

### *Priority*

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in United Kingdom on November 30, 1998. The certified copy of the 9826247.0 application as required by 35 U.S.C. 119(b) has been received and entered.

### *Claim Rejections - 35 USC § 102*

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 39, 40, 41, 42, 43, 44, 55, 56, 62, 89 and 91 are rejected under 35 U.S.C. 102(b) as being anticipated by Gossen et al. (USPN 5,602,300, 02/11/1997).

Gossen teach (claim 39) a method for at least partially separating nucleic acid molecules in a sample into populations wherein a population is tagged or capable of being tagged with a protein capable of being immobilized on a matrix, the method comprising contacting the nucleic containing sample with a matrix which selectively binds proteins whereby the said protein interacts directly with the matrix, whereby the tagged molecules are captured by the matrix and thereby separated from untagged molecules

(see col. 3 lines 1-7 and col. 4 lines 1-41, where the populations of DNA are genomic DNA and plasmid DNA, the protein is an antibody to the lacZ operater DNA, or LacI repressor protein, the LacI repressor or the antibody to the lacZ operator directly interacts with the solid particle which is the matrix).

With regard to claims 41,42, 89 and 91, Gossen teach the protein is a nucleic acid binding protein (see col. 4 line 22, where the LacI repressor is a DNA binding protein)

With regard to claim 43, Gossen teach the matrix is in the form of particles (see col. 4 lines 4-5).

With regard to claim 44, Gossen teach the matrix is a porous material (see col. 4 lines 4-5, where magnetic particles are porous).

With regard to claim 55, Gossen teach the nucleic acid molecules are separated into linear and circular DNA molecules (see col. 6 lines 41-49).

With regard to claim 56, Gossen teach further comprising introducing a tag to an end of the linear nucleic acid molecules, wherein said tag is a protein which is capable of being immobilized on a matrix, by direct interaction with the matrix and contacting the sample with a matrix which selectively binds proteins, whereby said tagged linear nucleic acid molecules are immobilized on the matrix (see col. 3 lines 1-7 and col. 4 lines 1-41, where the populations of DNA are genomic DNA and plasmid DNA, the protein is an antibody to the lacZ operater DNA, or LacI repressor protein).

With regard to claim 62, Gossen teach a method of separating linear from circular nucleic acid molecules in a sample said method comprising introducing a tag to an end of a linear nucleic acid molecule, wherein said tag is a protein which is capable of being immobilized on a matrix, by direct interaction with the matrix and contacting the sample with a matrix which selectively binds proteins whereby said tagged linear nucleic acid molecules are immobilized on the matrix (see col. 3 lines 1-7 and col. 4 lines 1-41 and col. 6 lines 41-49).

*Claim Rejections - 35 USC § 103*

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 45, 46, 80-86 and 93 rejected under 35 U.S.C. 103(a) as being unpatentable over Gossen et al. (USPN 5,602,300, 02/11/1997) as applied to claims 39, 43 and 44 above, and further in view of Seed (EP 0580305 A2, 01/26/1994).

The teachings of Gossen et al. are described previously and fully meet the limitations of claims 39, 41, 43 and 44.

Gossen et al. do not teach the matrix is incorporated into a separation device.

Seed teaches a matrix for separating nucleic acids is incorporated into a cartridge separation device (see example 1 lines 26-40). Additionally Seed teaches an absorbent pad is located on said porous material, a liquid impermeable sheet is located on the face of said absorbent pad remote from said porous material, and a liquid impermeable sheet having one or more holes therein is located on the face of said porous material remote from said absorbent pad, whereby the test sample is applied to one of said holes and is caused to diffuse transversely through said porous material by absorption into said absorbent pad (see example 1 lines 26-40).

One of ordinary at the time the invention was made would have been motivated to apply the method of separating nucleic acids as taught by Gossen et al. with the cartridge housed matrix as taught by Seed in order to increase the convenience and efficiency with which DNA is separated. Seed states, "This example demonstrates the use of coated substrates to purify plasmid DNA from rapid lysates....The resulting suspension was transferred to a cartridge similar to that described in example 1,

except that the cartridge also contained a cylindrical bundle of PHS-coated axially oriented polyester fibers... (see example 10 line 13-14 and 27-31)." It would have been prima facie obvious to apply the method of separating nucleic acids as taught by Gossen et al. with the cartridge housed matrix as taught by Seed in order to increase the convenience and efficiency with which DNA is separated. A single use cartridge housing the streptavidin bound matrix would be easy to store and use as exemplified by Seed.

5. Claims 47-54 rejected under 35 U.S.C. 103(a) as being unpatentable over Gossen et al. (USPN 5,602,300, 02/11/1997) as applied to claim 39 above, and further in view of Davis et al. (WO 90/12115, 10/18/1990).

The teachings of Gossen et al. are described previously and fully meet the limitations of claim 39.

Gossen et al. do not teach PCR of the separated DNA fragments, and detection of mutations in the amplified fragments.

Davis et al. teach PCR of DNA fragments and detection of mutations in the amplified fragments (see abstract, p. 24-31).

One of ordinary at the time the invention was made would have been motivated to apply the method of separating nucleic acids as taught by Gossen et al. with subsequent PCR and mutation detection as taught by Davis et al. in order to rapidly identify mutations in target DNA fragments. Davis et al state "By using the methods and products of this invention, it is possible to determine the genotype of an individual at any locus of interest. A single nucleotide position on a strand of DNA may be responsible for polymorphism or allelic variation. There are known disease states that are caused by such variation at a single nucleotide position. The usefulness of detecting such variation inculudes but is not limited to gene typing, karyotyping, genotyping, DNA family planning, diagnostics...(see p. 1). It would have been prima facie obvious to apply the method of separating nucleic acids as taught by Gossen et al. with subsequent PCR and mutation detection as taught by Davis

et al. in order to rapidly identify mutations in target DNA to use in applications such as for example, diagnostics, genotyping and prenatal testing.

6. Claims 47-54 rejected under 35 U.S.C. 103(a) as being unpatentable over Gossen et al. (USPN 5,602,300, 02/11/1997) as applied to claim 39 above, and further in view of Dower et al. (USPN 5,427,908, 06/27/1995).

The teachings of Gossen et al. are described previously and fully meet the limitations of claim 39.

Gossen et al. do not teach invitro packaging into bacteriophage particles.

Dower et al. teach invitro packaging into bacteriophage particles (see abstract).

One of ordinary at the time the invention was made would have been motivated to apply the method of separating nucleic acids as taught by Gossen et al. with invitro packaging into bacteriophage as taught by Dower et al. in order to rapidly screen a DNA library of interest. Dower et al. state "Methods are needed which facilitate the screening process, thereby enabling DNA sequences which encode proteins of interest and particularly antibody molecules to be more readily identified, recloned and expressed (see col. 1 lines 36-40)." It would have been prima facie obvious to apply the method of separating nucleic acids as taught by Gossen et al. with subsequent invitro packaging into bacteriophage as taught by Dower et al. in order to rapidly screen a DNA library of interest.

***Response to Arguments***

7. Applicant's arguments with respect to the 102 rejections have been considered but are moot in view of the new ground(s) of rejection.

Applicant's arguments with respect to the 103 (a) rejections have been fully considered to the extent they apply to the newly made rejections, but they are not persuasive. With respect to the rejections of claims 45 and 46 Applicant argues neither Seed or Ji teach or suggest the tag must be a protein or

interact directly with the matrix. This is not persuasive because Seed in not relied on for these teachings Gossen is relied on for these teachings as discussed in the new rejection detailed above. With respect to the rejections of claims 80-82, Applicants argue Seed uses only one membrane which is not liquid impermeable and that Seed relied on positive pressure to move the sample through the membrane. This is not persuasive because Seed teaches a liquid impermeable membrane (ie the Teflon sleeve). Seed discloses this sleeve as preventing leakage. Additionally, while Seed used positive pressure to force the liquid through the membrane, the liquid would eventually diffuse through the membrane without the use of positive pressure. Additionally, MPEP 2111.04 states,

> Claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure. However, examples of claim language, although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:
> (A) " adapted to " or "adapted for " clauses;
> (B) " wherein " clauses; and
> (C) " whereby " clauses.
> The determination of whether each of these clauses is a limitation in a claim depends on the specific facts of the case. In Hoffer v. Microsoft Corp., 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "whereby' clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention." Id. However, the court noted (quoting Minton v. Nat 'l Ass 'n of Securities Dealers, Inc., 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 003)) that a "whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.'" Id.

With respect to claims 57 and 58, Applicants argue Dover discloses the invitro packaging of nucleic acids into bacteriophage for the purpose of separating out particular DNA sequences and Dower do not teach of suggest the nucleic acids must be tagged with a protein or the tag interact directly with the matrix. This is not persuasive because Dower is not relied on for the teaching of the tag or the interaction of the tag with the matrix. Dower is relied on for the teaching of invitro packaging with bacteriophage. Applicants additionally argue the separation of the nucleic acids occurs before bacteriphage packaging wile in Dower the separation occurs after bacteriophage packaging. This is not persuasive because Dower is relied on simply to teach bacteriophage packaging of nucleic acids.

*Conclusion*

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

*Correspondence*

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

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